ABSTRACT OF THE DISCLOSURE

Lipidic compositions with superior characteristics for *in vivo* delivery of oligodeoxynucleotides (ODN) can easily and efficiently be made in the form of small multilamellar vesicles. The compositions contain a population of nucleic acid-containing lipid vesicles in a liquid carrier, and at least a portion of the lipid vesicles are small multilamellar vesicles. The small multilamellar vesicles are made from a lipid component including 20-30 mol % of an ionizable amino lipid such as DODAP, and a steric barrier lipid such as PEG-CerC_{14}; and an oligodeoxynucleotide contained in the lumen or interlamellar spaces of the small multilamellar vesicles. The ODN and lipid components are preferably present in the small multilamellar vesicles in a mole ratio of from 0.15 to 0.25. The compositions of the invention can be made by preparing two solutions: a lipid mixture with 20-30 mol % of the ionizable amino lipid, the steric barrier lipid and additional lipid components selected from among neutral lipids and sterols in an ethanolic solvent; and a solution of oligodeoxynucleotide in an aqueous solvent having a pH at which the ionizable amino lipid is positively charged. The lipid mixture is added to the solution of oligodeoxynucleotide to form a mixture containing lipid vesicles which is then massed through a filter to produce sized lipid vesicles in a solution containing ethanol. The ethanol is then removed, for example by dialysis. Then, the pH of the solution surrounding the sized lipid vesicles is increased to reduce the net positive charge on the exterior of the sized lipid vesicles.